

REMARKS

Prior to the present reply, claims 1-68 were pending. Due to a Restriction Requirement claims 1-52, 60, and 64-68 have been withdrawn from consideration. In the action mailed October 21, 2009, claims 53-59 and 61-63 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 53-57, 61, and 63 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,050,990 ("Tankovich"). Claims 58 and 59 are rejected under 35 U.S.C. § 102(b) as being anticipated or, in the alternative, under 35 U.S.C. § 103(a) as being obvious over Tankovich taken in light of U.S. Patent Application Publication No. 2003/0077823 ("Li") and PCT Publication No. WO 01/53461 ("Toma"). Claims 53-59 and 61-63 are also rejected under 35 U.S.C. § 103(a) as being obvious over Tankovich in view of Li and Toma. Each of these rejections is addressed below.

Claim amendments

Claims 53, 55, 57, 58, and 60 have been amended, and new claims 69-71 have been added. Claims 1-41 and 59 have been cancelled. Claim 53 has been amended to recite that the mammal is in need of skin regeneration, that the stem cells express nestin and fibronectin, that the stem cells do not express p75NTR and keratin 15. Support for these changes is found in original claims 58 and 59 and at page 25, line 10. Claims 53 and 60 have been amended to recite northern blot analysis, RT-PCR, western blot analysis, or immunohistochemical analysis. Support for this change is found, for example, at page 2, line 29, through page 3, line 1. Claim 55 has been amended to correct a minor typographical error. Claim 57 has been amended to recite that the cells are purified from the dermal papilla (DP) of a hair follicle. Claim 58 has been amended to correspond with the language of amended claim 1. Support for new claim 69 is found, for example, at page 4, line 16. Support for new claims 70 and 71 is found in original claims 53 and 54. These amendments add no new matter.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 53-59 and 61-63 are rejected as being indefinite. Claim 53 is rejected for requiring providing cells that “are capable of” regenerating skin, but for not requiring that the cells participate in the regeneration method. Claims 54-59 and 61-63 are rejected as depending from rejected claim 53. Claim 59 is also rejected as referring to “measurable levels” but for failing to point out the manner of measurement. Each of these matters is addressed below.

To address the rejection of claim 53 and its dependent claims, claim 53 has been amended to recite that the cells regenerate skin, thus making it clear that the cells participate in the regeneration method. This basis for rejection may be withdrawn.

The rejection of claim 59 is addressed as follows. Claim 59 has been cancelled, and its language has been incorporated into claim 53. Claim 53 has been further amended to recite that the manner of measurement is northern blot analysis, RT-PCR, western blot analysis, or immunohistochemical analysis. Amended claim 53 thus recites the manner of measurement. Withdrawal of this rejection is likewise requested.

Rejection under 35 U.S.C. § 102(b) - Tankovich

Claims 53-57, 61, and 63 are rejected as being anticipated by Tankovich. The Office relies upon Tankovich as teaching isolating skin containing DP, separating stem cells from the skin, cloning the cells (i.e., culturing them to homogeneity), and grafting the cells into an incision on a desired area on the patient’s head. The Office interprets the incision as being “damaged skin.”

For a reference to anticipate a claim, the reference must teach every limitation of that claim. Because Tankovich does not teach every limitation of amended claim 53, this reference cannot anticipate this claim or its dependent claims.

Amended claim 53 requires that the mammal be in need of skin regeneration. Tankovich only describes individuals undergoing hair transplantation, and the incisions of

Tankovich are being made solely to transplant cells for the purpose of hair transplantation. Accordingly, these individuals of Tankovich are not in need of skin regeneration. Tankovich thus fails to teach this claim limitation and cannot anticipate claims 53-57, 61, and 63.

Further, the cells described in Tankovich derive from a different portion of the hair follicle than those of the present claims and are thus a distinct cell population. While Tankovich suggests that hair follicle stem cells derived from either the bulge area or the papilla can be used to stimulate hair growth (column 56, lines 25-27), Tankovich only describes isolation of bulge area cells (column 56, lines 27-31; column 56, lines 48-49; and column 57, lines 37-41 of Tankovich). The claimed cells, by contrast, are not found in the bulge area (see, e.g., page 20, lines 22-26 of the specification), but rather are found in the DP and in the dermal sheath (see page 2, lines 9-10, and page 14, lines 12-15 of the specification). Indeed, the specification makes it clear that stem cells from the bulge are epidermal stem cells (page 22, line 25), in contrast to the dermal stem cells of the present claims. Thus, cells of the present invention do not derive from the portion of the hair follicle described in Tankovich. Tankovich thus does not teach use of the claimed cells and cannot anticipate claim 53 or its dependent claims for this reason.

Even if Tankovich suggests using cells from the DP, there is no disclosure of multipotent stem cells derived from the DP. Multipotent stem cells have two critical characteristics: the ability to differentiate into different types of cells and the ability to self-renew. Cultured DP cells described in the literature do not have the ability to self-renew, and their ability to induce hair growth over time. For example, Rendl et al., *Genes Dev* 22:543-557, 2008 ("Rendl"; attached as Exhibit A) teaches that DP cells lose their ability to induce hair follicle formation when cultured (see Abstract and page 544, left column, 3rd full paragraph). Rendl therefore focuses on identification of growth factors, such as BMPs, that can maintain the ability of the DP cells to induce hair follicle formation. However, even treatment with BMP alone was not sufficient to maintain hair

follicle inducing ability in cultured DP cells (see, e.g., Summary on page 554). Because cultured DP cells described in Rendl and elsewhere do not maintain their ability to differentiate in culture over time, cultured DP cells, generally, do not constitute populations of multipotent stem cells. Thus, Tankovich cannot be said to teach (or even suggest) the population of multipotent stem cells recited in the present claims. For this reason as well, Tankovich cannot anticipate claim 53 or its dependent claims.

Withdrawal of the § 102(b) rejection over Tankovich is respectfully requested.

Rejection under 35 U.S.C. § 102(b) or 103(a) – Tankovich in light of Li and Toma

Claims 58 and 59 are rejected as being anticipated by Tankovich, or, in the alternative, obvious over Tankovich in light of Li and Toma. The rejection these claims as being anticipated by Tankovich is respectfully traversed for the reasons set forth above.

The rejection of claims 58 and 59 as being obvious over Tankovich in light of Li and Toma is traversed for the reasons set forth below.

Rejection under 35 U.S.C. § 103(a) – Tankovich in light of Li and Toma

Claims 53-59 and 61-63 are rejected as being obvious over Tankovich in light of Li and Toma. The teachings of Tankovich are explained above. Li is cited as teaching a population of nestin-expressing cells in hair follicles that can regenerate skin. Toma is cited as teaching a population of stem cells isolated from skin that express nestin but do not express p75 NTR. Based on these combined teachings, the Office infers that the cells of Tankovich express nestin but not p75 NTR and that these cells can be used to regenerate skin. Applicants respectfully traverse this rejection.

To find a claim obvious, “there must be some articulated reasoning with some rational underpinning to support a legal conclusion of obviousness.” *KSR v. Teleflex*, 550 U.S. 398, 418; 82 U.S.P.Q.2d 1385, 1396. As none of the cited references provide any

basis for concluding that the claimed cells can regenerate skin, these references cannot render the claimed method obvious.

Neither Tankovich nor Li teach the cells recited in the claims

As explained above, Tankovich teaches isolation and culturing of bulge-derived stem cells. These cells include epidermal stem cells, which are distinct from the dermally-derived cells of the present claims. Indeed, the present specification indicates that the claimed cells are not found in the bulge region. Thus, Tankovich does not teach the claimed cells.

Li fails to remedy the deficiency of Tankovich. The cells of Li, like those of Tankovich, also derive from the bulge region. Indeed, as explained in paragraph 11 of Li, the nestin-GFP cells were located exclusively in the bulge area. Li further explains that the stem cells express keratin 15, as explained in paragraph 47. The present cells, by contrast, do not express keratin 15, as recited in claim 53, and are found in the DP. Thus, neither Li nor Tankovich teach a population of multipotent stem cells that express the claimed markers. For these reasons, neither Tankovich nor Li can form the basis for rendering claim 53 or its dependent claims obvious.

Toma teaches a different population of cells from that of Tankovich and Li

Tankovich and Li, as explained above, teach a population of cells different from those presently claimed. The cells of Tankovich and Li are also distinct from those of Toma. Toma teaches multipotent stem cells derived from peripheral tissue, including skin, of juvenile and adult mammals (see page 3, lines 19-23, of Toma) and that these cells are dermally derived (page 6, lines 12-26 of Toma). Toma also teaches that these cells can differentiate into dopaminergic neurons, smooth muscle cells, adipocytes, cardiac muscle cells, pancreatic islet cells, hematopoietic cells, and hepatocytes (page 3, line 27 to page 4, line 4). Li and Tankovich, by contrast, describe cells derived from the

hair follicle bulge region, which, as noted above, contains epidermal stem cells. Thus, Toma teaches a population of cells different from those described in Tankovich or Li. For this reason, the teachings of Li and Tankovich cannot be combined with those of Toma to arrive at the present invention.

Neither of Tankovich nor Toma teaches skin regeneration

Finally, neither Tankovich nor Toma teaches or suggests regenerating skin. As explained above, Tankovich is focused on hair regeneration. Toma is silent with respect to regenerating skin. Thus, these references cannot form the basis for rendering the present claims obvious for this reason as well.

No combination of these references leads one to the present invention

Tankovich and Li each fail to teach the claimed stem cells, and Tankovich and Toma fail to teach regeneration of skin. Thus, these references provide no basis or reason for using the claimed cells to regenerate skin. Absent such a reason, these references cannot render claim 53 or its dependent claims obvious. Withdrawal of the rejection under § 103(a) is respectfully requested.

CONCLUSION

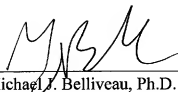
Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a Petition to extend the period for replying to the Office action for three (3) months, to and including April 21, 2010, and authorization to charge Deposit Account No. 03-2095 in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit
Account No. 03-2095.

Respectfully submitted,

Date: _____

4.9.10



Michael J. Belliveau, Ph.D.
Reg. No. 52,608

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045